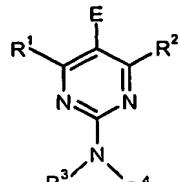


## CLAIMS

1. A process for the preparation of a compound of Formula (1):



5 Formula (1)

which comprises

- a) reacting a compound of formula  $R^1\text{-CO-CH}_2\text{-E}$  with a compound of formula  $R^2\text{-CHX}^1\text{X}^2$  in the presence of a compound of formula  $R^3R^4\text{N-C(=NH)NH}_2$  and a catalyst, thereby to form a dihydropyrimidine; and
- 10 b) oxidising the dihydropyrimidine produced in step a) to form the compound of Formula (1)

wherein

$R^1$  is H or an alkyl group;

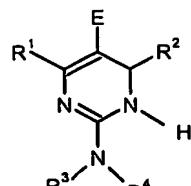
15  $R^2$  is H or an alkyl or aryl group;

$R^3$  and  $R^4$  are each independently H, alkyl or aryl, or  $R^3$  and  $R^4$  are linked to form, together with the nitrogen to which they are attached to form a 5 to 7 membered heterocyclic ring;

$E$  is H, an unsubstituted alkyl group, an aryl group or an electron withdrawing group; and

20  $X^1$  and  $X^2$  are each independently leaving groups, or  $X^1$  and  $X^2$  together represent =O.

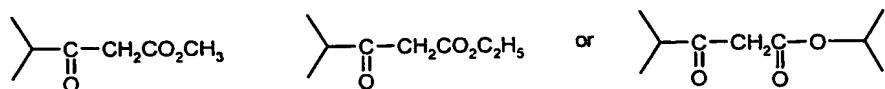
2. A process according to claim 1, wherein the dihydropyrimidine is represented by the Formula (2a), and tautomers thereof:



25 Formula (2a)

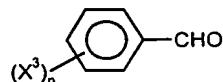
wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$  and  $E$  are as defined in claim 1.

30 3. A process according to claim 1 or claim 2, wherein the compound of formula  $R^1\text{-CO-CH}_2\text{-E}$  is a compound of formulae:



4. A process according to any preceding claim, wherein the compound of formula  $R^2\text{-CHX}^1\text{X}^2$  is a compound of formula:

5



wherein  $X^3$  represents halo, and  $n$  is 0 or 1-5, and preferably 4-fluorobenzaldehyde.

10 5. A process according to any preceding claim, wherein the compound of formula  $R^3\text{R}^4\text{N-C(=NH)NH}_2$  is guanidine or methylguanidine.

6. A process according to claim 5, wherein the compound of formula  $R^3\text{R}^4\text{N-C(=NH)NH}_2$  is employed as a hydrochloride or sulfate salt.

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7. A process according to any preceding claim, wherein the catalyst is a base.

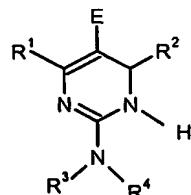
8. A process according to claim 7, wherein the base is an alkali or alkaline earth metal carbonate or hydrogencarbonate.

20

9. A process according to any preceding claim, wherein the oxidising agent is manganese dioxide.

10. A compound of Formula (2a), and tautomers thereof:

25



Formula (2a)

wherein

$R^1$  is H or an alkyl group;

30  $R^2$  is H or an alkyl or aryl group;

$R^3$  and  $R^4$  are each independently H, alkyl or aryl, provided that  $R^3$  and  $R^4$  are not both unsubstituted alkyl; and

E is an unsubstituted alkyl group, an aryl group or an electron withdrawing group, further provided that R<sup>1</sup> is not -CH<sub>3</sub> when R<sup>2</sup> is unsubstituted phenyl or o-nitrophenyl.

11. A compound according to claim 10, wherein R<sup>2</sup> represents a phenyl group substituted by one or more halogens.

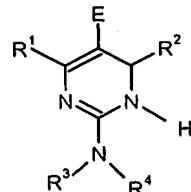
5 12. A compound according to claim 10 or 11, wherein at least one of R<sup>3</sup> and R<sup>4</sup> is H.

13. A compound according to any one of claims 10 to 12, wherein R<sup>1</sup> represents isopropyl and R<sup>2</sup> represents 4-fluorophenyl.

10 14. A compound according to any one of claims 10 to 13, wherein R<sup>3</sup> is H or methyl and R<sup>4</sup> is H.

15 15. A compound according to anyone of claims 10 to 14, wherein E represents a group of formula -CO<sub>2</sub>(C<sub>1-4</sub>alkyl).

16. A process for the preparation of a compound of Formula (2a) and tautomers thereof:



20 Formula (2a)

which comprises

a) reacting a compound of formula R<sup>1</sup>-CO-CH<sub>2</sub>-E with a compound of formula R<sup>2</sup>-CHX<sup>1</sup>X<sup>2</sup> in the presence of a compound of formula R<sup>3</sup>R<sup>4</sup>N-C(=NH)NH<sub>2</sub> and a catalyst, thereby to form the compound of Formula (2a)

25 wherein

30 R<sup>1</sup> is an H or an alkyl group;

R<sup>2</sup> is an H or an alkyl or aryl group;

R<sup>3</sup> and R<sup>4</sup> are each independently H, alkyl or aryl, or R<sup>3</sup> and R<sup>4</sup> are linked to form, together with the nitrogen to which they are attached to form a 5 to 7 membered heterocyclic ring;

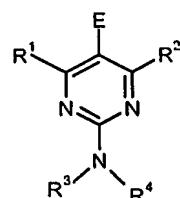
E is H, an unsubstituted alkyl group, an aryl group or an electron withdrawing group; and X<sup>1</sup> and X<sup>2</sup> are each independently leaving groups, or X<sup>1</sup> and X<sup>2</sup> together represent =O.

17. A process according to claim 16, wherein  $R^1$  represents isopropyl,  $R^2$  represents 4-fluorophenyl, and  $R^3$  and  $R^4$  each independently represents H or methyl.

18. A process according to claim 17, wherein  $R^3$  is methyl and  $R^4$  is H.

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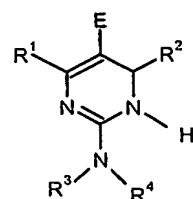
19. A process for the preparation of a compound of Formula (1):



Formula (1)

10

which comprises oxidising a compound of Formula (2a):



Formula (2a)

15 wherein

$R^1$  is H or an alkyl group;

$R^2$  is an H, an alkyl or aryl group;

$R^3$  and  $R^4$  are each independently H, alkyl or aryl, or  $R^3$  and  $R^4$  are linked to form, together with the nitrogen to which they are attached to form a 5 to 7 membered

20 heterocyclic ring; and

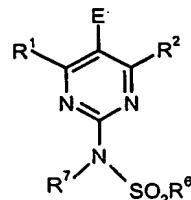
E is H, an unsubstituted alkyl group, an aryl group or an electron withdrawing group.

20. A process according to claim 19, wherein  $R^1$  represents isopropyl,  $R^2$  represents 4-fluorophenyl, and  $R^3$  and  $R^4$  each independently represents H or methyl.

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21. A process according to claim 19 or 20, wherein the oxidation employs manganese dioxide.

22. A process for the preparation of a compound of Formula (3):

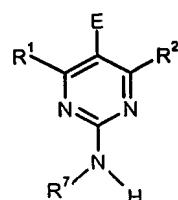


Formula (3)

5 which comprises

- a) reacting a compound of formula  $R^1\text{-CO-CH}_2\text{-E}$  with a compound of formula  $R^2\text{-CHX}^1\text{X}^2$  in the presence of a compound of formula  $R^7\text{HN-C(=NH)NH}_2$  and a catalyst, thereby to form a dihydropyrimidine;
- b) oxidising the dihydropyrimidine produced in step a) to form a compound of Formula (4)

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Formula (4)

and

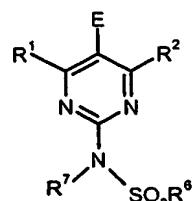
- c) reacting the compound of Formula (4) with a compound of formula  $R^6\text{SO}_2\text{-X}^4$  to give a compound of Formula (3);

15 wherein

- $R^1, R^2, E, X^1$  and  $X^2$  are as defined in claim 1;
- $R^6$  represents alky or aryl, preferably methyl;
- $R^7$  is H, alkyl or aryl; and

20  $X^4$  represents a leaving group, preferably Cl or Br.

23. A process for the preparation of a compound of Formula (3):



Formula (3)

25

which comprises

a) reacting a compound of formula  $R^1\text{-CO-CH}_2\text{-E}$  with a compound of formula  $R^2\text{-CHX}^1X^2$  in the presence of a compound of formula  $R^7\text{HN-C(=NH)NH}_2$  and a catalyst, thereby to form a dihydropyrimidine comprising an exocyclic group formula  $\text{-NHR}^7$ ;

5 b) reacting the compound of Formula (4) with a compound of formula  $R^6\text{SO}_2\text{-X}^4$  to form a dihydropyrimidine comprising an exocyclic group formula  $\text{-N(R}^7\text{)SO}_2\text{R}^6$ ;

c) oxidising the dihydropyrimidine produced in step b) to form a compound of Formula (3);  
wherein

$R^1$ ,  $R^2$ ; E,  $X^1$  and  $X^2$  are as defined in claim 1;

10  $R^6$  represents alky or aryl, preferably methyl;

$R^7$  is H, alkyl or aryl; and

$X^4$  represents a leaving group, preferably Cl or Br.

15 24. A process according to claim 22 or 23, wherein  $R^1$  represents isopropyl,  $R^2$  represents 4-fluorophenyl,  $X^1$  and  $X^2$  together represent  $=\text{O}$ ,  $R^6$  represents methyl, E represents a group of formula  $\text{-CO}_2(\text{C}_{1-4}\text{alkyl})$ , and  $R^7$  is H or methyl.

25. A compound of formula  $(\text{CH}_3)_2\text{CH-CO-CH}_2\text{-CO}_2\text{-C}_3\text{H}_7$

20 26. A compound according to claim 25, of formula:

